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EXAMINER	
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1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/512,004	TZARTOS ET AL.	
	Examiner	Art Unit	
	Chang-Yu Wang	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-41* is/are pending in the application.

4a) Of the above claim(s) *28-35 and 37-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-27 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 October 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Sequence compliance

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821 (a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. § 1.821 through 1.825. Specifically, no sequence identification has been provided for the nucleic acid sequences presented at p. 10, lines 31-33, p. 13, lines 12-21, line 34, p. 14, lines 24-25 and p. 17, lines 7-10 of the instant specification. In case these sequences are new, Applicant needs to provide a substitute computer readable form (CRF) copy of a "Sequence Listing" which includes all of the sequences that are present in the instant application and encompassed by these rules, a substitute paper copy of that "Sequence Listing", an amendment directing the entry of that paper copy into the specification, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. § 1.821 (e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). The instant specification will also need to be amended so that it complies with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. See M.P.E.P. 2422.04.

Status of Application/Election/Restrictions

2. Applicant's election with traverse of Group I (claims 11-27 and 36) in the reply filed on 7/14/08 is acknowledged. The traversal is on the ground(s) that the species election is improper because the claims are directed to use of a combination of recombinant domains (alpha-epsilon). This is found persuasive. Thus, the species election with regard to different subunits is withdrawn. The subject mater to the extent of the recited subunits will be examined in this office action.

The requirement for the rest of restriction is still deemed proper and is therefore made FINAL.

3. Claims 11-41 are pending. Claims 28-35 and 37-41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 11-27 and 36 are under examination in this office action.

Priority

4. Should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d) prior to declaration of an interference, a certified English translation of the foreign application must be submitted in reply to this action. 37 CFR 41.154(b) and 41.202(e).

Failure to provide a certified translation may result in no benefit being accorded for the non-English application.

Specification

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The elected invention is directed to a method of immunoadsorption of anti-AChR antibodies using a combination of recombinant domains of nicotinic acetylcholine receptor (AChR) subunits.

Claim Objections

6. Claims 16 and 24 are objected to because of the following informalities: Pichia pastoris recited in claim 24 is a strain of yeast so it should be italic. In addition, SFV recited in claim 24 and P3A recited in claim 16 are not a common abbreviation. Applicants are required to spell out SFV and P3A at the first usage. Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 11-27 are indefinite because the claims recite “a combination of recombinant domains derived from any one of alpha…subunits of the primate muscle

nicotinic acetylcholine receptor (AChR). The claims fail to define the corresponding positions for the subunit of AChR. It is unclear to a skilled artisan as to what amino acid residues or sequences are encompassed within the claimed recombinant domains of the recited AChR subunit and thus within the scope of the claims. One of skill in the art cannot determine the sequences of the claimed domains, which renders the claims indefinite. In addition, the recitation "derived from" makes claims indefinite because the claims and the disclosure fail to set forth the metes and bounds of what is encompassed within the definition of a recombinant domain "derived from…".

In addition, claims 16 and 24 are indefinite because of the terms "P3A" and "SFV" recited in the claims without a reference to a precise amino acid sequence identified by a proper SEQ ID NO: or providing a full name for abbreviated names. Without identification of property or combination of properties which are unique to and, therefore, definitive of the instant recitations, the metes and bounds of the claims remain undetermined. Further, the use of laboratory designations only to identify a particular molecule renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct molecules. The rejection can be obviated by amending the claims to specifically and uniquely identify P3A or SFV, for example, by SEQ ID NO. and function of P3A or SFV.

8. Claims 16, 18-22 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: specific sequences.

The claims only recite different amino acid residues. However, it is not clear what specific sequences that Applicant intended to use or refer to, which renders the claims indefinite.

Claim Rejections - 35 USC § 112-2nd & 101

9. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 11-27 provide for the use of a combination of recombinant domains derived from any one of the alpha, beta, gamma, delta and epsilon subunits of primate muscle nicotinic acetylcholine receptor (AChR), but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 11-27 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-27 and 36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

Claims 11-27 and 36 are drawn to a method of immunoadsorption of anti-AChR antibodies using a combination of recombinant domains derived from any one of the alpha, beta, gamma, delta and epsilon subunits of the primate muscle nicotinic acetylcholine receptor (AChR) or mutant forms of the recombinant domains. The claims encompass use of a genus of recombinant domains derived from any one of the alpha, beta, gamma, delta and epsilon subunits of the AChR and also encompass use of a genus of mutant forms of the recombinant domains. In addition, the claims also encompass use of structurally and functionally undefined N-terminal domains, in particular claims 16-22 and 25.

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant is in possession of and what Applicant is claiming. From the specification, it is clear that Applicant is in possession of known defined full length sequences of human alpha 1-210, gamma 1-218 and epsilon 1-219 sequences to be used in the claimed method. However, the claims are not limited to the sequences as set forth above. The claims recite any recombinant domains derived from any subunit of AChR. The claims also recite the recombinant domains comprising the structurally and functionally undefined N-terminal domain. Applicant is not in possession of such broad genus of derivatives and structurally and functionally undefined domains to be used in the claimed method. The specification fails to teach or identify what particular portion of the structure that must be conserved in the claimed genus of recombinant domain comprising the N-terminal domain. The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus. There is no description of the conserved regions which are critical to the function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure of recombinant domains or its derivatives to the function of the defined full length subunit sequences. In addition, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify all forms of derivatives and recombinant domains and what these domains might be. Since the common characteristics/features of all forms of recombinant domain derivatives are

unknown, a skilled artisan cannot envision functional correlations of the genus with the claimed invention. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the genus of proteins.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, the claimed method of using a structurally and functionally undefined recombinant domains in immunoadsorption of anti-AChR has not met the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement. See MPEP § 2163.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11-21, 23-27 and 36 are rejected under 35 U.S.C. 102 (a) as being anticipated by Psaridi-Linardaki et al. (J. Biol.Chem. 2002. July, 277:2698-26986).

Claims 11-21, 23-27 and 36 are directed to a method of immunoadsorption of anti-AChR antibodies or removal of anti-AChR antibodies of the blood of myasthenia graivs patients by using a combination of recombinant domains from any one of the alpha, beta, gamma, delta and epsilon subunits of the primate muscle nicotinic acetylcholine receptor (AChR).

Psaridi-Linardaki et al. teach a method of immunoadsorption of anti-AChR antibodies of myasthenia gravis (MG) patients using a combination comprising a recombinant domain of human alpha 1-210 or using a combination comprising a solubilized hybrid AChR HαTβγδ containing human α and Torpedo β, γ and δ subunits (see p. 26984, 1st -2nd cols., in particular). The recombinant domains of the human alpha 1-210 or the solubilized hybrid meet the limitations of a combination comprising different subunits that contain the N-terminal extracellular domain comprising recited amino acids of α, β, γ and δ subunits as recited in instant claims 11-14 and 17-21,25 and 26 (see p. 26984, 1st -2nd col., in particular). In addition, Psaridi-Linardaki et al. teach the recombinant domains are expressed in yeast Pichia pastoris expression system as recited in instant claims 23-24 (see p. 26981, 1st col., 4th paragraph, in particular). Furthermore, Psaridi-Linardaki et al. teach removal of anti-AChR antibodies from the blood (i.e. serum) of MG patients using the claimed recombinant domains as recited in instant claims 27 and 36 (see p. 26981, 2nd col., 7th paragraph; p. 26984, 1st col., 3rd paragraph to col.2, 1st paragraph, in particular). Therefore, Claims 11-21, 23-27 and 36 are anticipated by Psaridi-Linardaki et al..

12. Claims 11-18, 23 and 25-26 are rejected under 35 U.S.C. 102 (b) as being anticipated by Barchan et al. (Eur. J. Immunol.1998. 28: 616-624).

Claims 11-18, 23 and 25-26 are directed to a method of immunoadsorption of anti-AChR antibodies by using a combination of recombinant domains from any one of the alpha, beta, gamma, delta and epsilon subunits of the primate muscle nicotinic

acetylcholine receptor (AChR) wherein the recombinant domains are mutant forms of the domains including substitutions of free cysteine by other amino acids or substitutions of the hydrophobic loops of the subunits 128-142 or alpha domain of containing P3A axon or a FLA tag at the N-terminus.

Barchan et al. teaches a method of immunoadsorption of anti-AChR antibodies using a combination of recombinant domains from human alpha subunit Hα1-210 or Hα1-121 or Hα122-210, which meet the limitations of claims 11-14, 17, 18, 23, 25 and 26 (see p. 616, abstract; p.617, 2nd col. to p.619, 2nd col., in particular). Barchan et al. also teaches that the human alpha subunit exist two forms including 25-additional amino acid insertion between position 58 and 59 as encoded by exon p3A (see p. 617, 2nd col.; p. 620, 2nd col. to p. 621, 2nd col., in particular), which meets the limitations recited in instant claims 15-16. Thus, claims 11-18, 23 and 25-26 are anticipated by Barchan et al..

13. Claims 11-14, 17-18, 23, 25-27 and 36 are rejected under 35 U.S.C. 102 (b) as being anticipated by US Patent No. 5578496 (cited previously).

Claims 11-14, 17-18, 23, 25-27 and 36 are directed to a method of immunoadsorption of anti-AChR antibodies or removal of anti-AChR antibodies of the blood of myasthenia graivs patients by using a combination of recombinant domains from any one of the alpha, beta, gamma, delta and epsilon subunits of the primate muscle nicotinic acetylcholine receptor (AChR).

US Patent No. 5578496 (the '496 patent) teaches a method of immunoadorption using a recombinant AChR-α subunit as recited in instant claims 11-14, 17-18, 23, 25-27 and 36. The '496 patent teaches a method of immunoadsorption of anti-AChR antibodies in the blood (serum) of myasthenia gravis (MG) patients using a combination comprising a recombinant domain of human AChR alpha 1-210 or using a combination comprising human α subunit peptides (see abstract; col. 23, line 15-col. 24, line 15; col.25-26, example V; col. 27, line 1-col. 29, line 27; col. 43, claims 1-6, in particular). The recombinant domains of the human alpha 1-210 or peptides meet the limitation of a combination comprising recombinant domains derived from the N-terminal extracellular domain of AChR alpha-subunit as recited in instant claims 11-14, 17-18, 23, 25-26 (see col. 18-20; col. 27-28, in particular). The '496 patent teaches removal of anti-AChR antibodies from the serum (i.e. derived from the blood) of MG patients using the claimed recombinant domains as recited in instant claims 27 and 36 (see col. 25, example V; col.27-29, in particular). Thus, Claims 11-14, 17-18, 23, 25-27 and 36 are anticipated by US Patent No. 5578496.

14. Claims 11-14, 17-23, 25-27 and 36 are rejected under 35 U.S.C. 102 (b) as being anticipated by Besson et al. (Neurology, 1996. 47:1552-1555).

Besson et al. teach a method of immunoadsorption of anti-AChR antibodies in the blood from MG patients using a combination comprising a recombinant domain of alpha, beta, gamma, delta, epsilon subunits of human AChR as recited in instant claims 11-14, 17-23, 25-27 and 36 (see p. 2-3). Besson et al. teach that recombinant domains

of AChR subunits extracted from TE671-epsilon and TE671-gamma cell lines (see p. 2-3). The TE671-epsilon and TE671-gamma cell lines are TE671 cell lines that are transfected with AChR epsilon and gamma subunit respectively. TE671 cell lines also express AChR alpha, beta and delta subunits. Besson et al. also teach using the recombinant domains of different AChR subunits extracted from TE671-epsilon and –gamma cell lines for immunoadsorption of anti-AChR antibodies in the blood from MG patients, which meet the limitations as recited in the claims 27 and 36 (see p. 3-4). The recombinant domains of different AChR subunits comprise the N-terminal domain of each subunit and also comprise the recited amino acids as in claims 17-22. In addition, these recombinant domains are expressed in TE671 cell lines, which is a eukaryotic expression system and are also larger than 70 amino acids as recited in instant claims 23, 25-26. Thus, Claims 11-14, 17-23, 25-27 and 36 are anticipated by Besson et al..

Conclusion

15. NO CLAIM IS ALLOWED.

16. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

US2002/008652 teaches a method of immunoadsorption of anti-AChR antibodies in MG patients using a combination comprising recombinants human AChR alpha subunits.

17. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday from 8:30 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/CYW/
Chang-Yu Wang, Ph.D.
October 18, 2008

/Christine J Saoud/
Primary Examiner, Art Unit 1647